REMARKS

Claims 16-37 are pending in this application and are rejected by the final Office Action identified above. Applicant submits minor amendments to claims 16 and 28. Specifically, claim 16 is amended to clarify that the control amplification reaction and the previous amplification reaction are conducted in different samples. Applicant respectfully submits that such an amendment merely makes more explicit the difference between the "control nucleic acid amplification reaction" and the "previous amplification reaction," both of which are pre-existing claim terms. Similarly, claim 28 is amended to clarify that the second nucleic acid sample is different from the first nucleic acid sample. Applicant submits that these amendments provide no new grounds for rejection since they merely clarify the presently claimed invention, as discussed in more detail below. Applicant also submits that no new matter is added through these amendments. Therefore, Applicant respectfully requests the entry of the proposed amendments.

Upon entry of the present Amendment, claims 16-37 are still pending and presented for reconsideration.

The undersigned wishes to thank the Examiner for her time and courtesy during the telephonic interview that took place earlier on this day. The following remarks are intended to constitute a proper recordation of such interview in accordance with MPEP § 713.04, and also to provide a full response to the Office Action mailed on December 2, 2002.

Rejections Under 35 U.S.C. § 102

Claims 16, 18, 19, 21-23, 25, 28, 29, 31-34, and 37 are rejected under 35 U.S.C. § 102 as being anticipated by WO 91/15601 (hereinafter "Shuldiner"). Among those claims, claims 16 and 28 are the only independent claims.

Shuldiner describes an amplification method that distinguishes cDNA made from endogenous RNA in a sample from contaminating DNA in the same sample and amplifies only the endogenous RNA sequences (pg. 6, lns. 23-27). Specifically, the method involves using a hybrid primer containing a 5'-unique random sequence in a reverse transcripti n, resulting in DNA tagged with the unique random sequence (pg. 7,

lns. 22-29). Subsequently, a primer specific for the random sequence is used in a PCR reaction conducted in the same sample containing the tagged DNA in order to selectively amplify the tagged DNA (pg. 8, lns. 14-17, and 26-27).

Shuldiner does not teach or suggest the methods recited in amended claims 16 and 28 for detecting cross-sample contamination in amplification reactions. The Examiner states in the final Office Action that the method of Shuldiner can be used in the detection of cross-sample contamination. Applicant respectfully traverses. According to Shuldiner's method, after the reverse transcription, the DNA tagged with the unique random sequence is positively amplified. Because none of the contaminating DNA is tagged, Shuldiner's method does not perform the last step recited in either amended claim 16 or amended claim 28, which is determining whether contamination has taken place. Shuldiner's method amplifies the target template regardless whether there is any contamination in its sample. Obtaining an amplicon using Shuldiner's method does not give one any information on whether there is contamination in the sample or not.

Moreover, the amplification reactions in Shuldiner's method have to be conducted in the same sample, as it avoids possible contaminating DNA by amplifying only sequences derived from endogenous RNA in the same sample (pg. 8, lns. 26-27). The Examiner states in the final Office Action that the pending claims do not recite that the samples are different. Applicant submits that by reciting a step of determining whether a sample has been contaminated by another sample, the original claims 16 and 28 each recite a method that one of ordinary skill would understand to require two different samples, because a sample cannot "contaminate" itself. However, in the interest of advancing prosecution, Applicant submits clarifying amendments to claims 16 and 28 to explicitly recite different samples in each claimed method. Thus, as already discussed in a previous Response dated August 30, 2002, Shuldiner not only fails to teach or suggest determination of contamination, but also fails to teach or suggest detection of cross-sample contamination.

Accordingly, Applicant respectfully submits that Shuldiner does not supply a sufficient basis for a rejection of the pending claims under 35 U.S.C. § 102. Therefore, Applicant respectfully requests that all rejecti ns under § 102 be reconsidered and withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 24, 26, 27, 35, and 36 are rejected under 35 U.S.C. § 103 (a) as being obvious over Shuldiner in view of U.S. Pat. No. 4,965,188 to Mullis et al. (hereinafter "Mullis").

As described above, Shuldiner does not teach or suggest detection of cross-sample contamination as presently claimed. Mullis describes general methods for amplifying a target nucleic acid sequence in a nucleic acid mixture. *See* Abstract. Its methods use two primers that are complementary to portions of the two strands of a target sequence, but it does not teach or suggest any method for detecting contamination in an amplification reaction. Therefore, the combination of the two references fails to disclose or suggest all the claim elements. Accordingly, Applicant respectfully submits that the 35 U.S.C. § 103 rejections cannot be sustained against the pending claims. Therefore, Applicant respectfully requests that all rejections under § 103 be reconsidered and withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 17, 20, and 28-37 were rejected under 35 U.S.C. § 112, second paragraph, for failing to set forth the subject matter which Applicant regards as his invention.

a. The Examiner states in the final Office Action that claim 20 is vague because of the language "one primer in said control reaction further comprises an additional sequence 3' to said detection sequence." The Examiner further asks whether the language means the primer comprises an additional sequence at the 3' end. Applicant submits, without amendment to the claim, that the phrase "3' to" in the quoted language indicates the position of the recited "additional sequence" relative to "said detection sequence." In other words, the "additional sequence" is closer to the 3' end of the primer than "said detection sequence" is. Accordingly, claim 20 includes the situation where the "additional sequence" is at the 3' end of the primer.

b. The Examiner states that claims 28-37 are vague and indefinite because the language "the amplification f which is desired," in claim 28, is unclear as to which amplification it is referring to. Applicant submits, without amendment to claim 28, that

the quoted phrase modifies the "target nucleic acid" that precedes the quoted phrase. In other words, the amplification of the "target nucleic acid" is desired.

c. The Examiner states that it is unclear what is meant by "at least one primer in said control reaction is not complementary to any contiguous nucleic acid sequence in said template" in claims 17 and 30. Applicant submits, without amendment to the claims, and as put forward in the previous Response dated August 30, 2002, that neither primer recited in claims 17 or 30 is complementary to any continuous stretch of nucleic acid sequence in a target template, although separate parts of the target template, say, two nucleotides here and three nucleotides there, may together be complementary to part or all of the primer sequence.

In light of the foregoing reasons, Applicant respectfully submits that the existing language of claims 17, 20, and 28-37 is clear and definite to one skilled in the art, and respectfully submits that the rejections under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

Summary

Applicant respectfully requests that the Examiner reconsider the application and claims in light of the foregoing Amendment and Response, and respectfully submits that the pending claims are in condition for allowance. If the Examiner believes that a second telephonic interview would expedite the favorable prosecution of the Application, the undersigned attorney would welcome the opportunity to work with the Examiner toward placing the Application in condition for allowance.

Respectfully submitted,

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Reg. No. 41,418

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MARKED-UP COPY OF AMENDED CLAIMS

16. (Amended) A method for detecting contamination by an amplicon from a previous amplification reaction, said method comprising the steps of:

conducting a control nucleic acid amplification reaction in a sample in a control sample comprising a nucleic acid template, using at least one primer that is capable of amplifying a detection sequence but not said template, said detection sequence having been incorporated in an amplicon of a previous amplification reaction conducted in a sample different from said control sample, using at least one chimeric primer comprising said detection sequence at a 5' end of said at least one chimeric primer; and

determining whether said sample has been contaminated by said previous amplification reaction by determining whether said control reaction produces an amplicon.

28. (Amended) A method for detecting contamination by an amplicon from a previous sample, said method comprising the steps of:

conducting an amplification reaction in a first nucleic acid sample, using at least one chimeric primer comprising a first portion that hybridizes with at least a portion of a target nucleic acid, the amplification of which is desired, and a second, contamination detection portion that does not hybridize with said target nucleic acid;

conducting a control amplification reaction in a second nucleic acid sample different from said first nucleic acid sample, using at least one primer to amplify specifically said contamination detection portion of said chimeric primer; and

determining whether said second sample has been contaminated by an amplicon from said first sample by determining whether said control reaction produces an amplicon.

CLEAN COPY OF PENDING CLAIMS

1-15. (Canceled)

16. (Amended) A method for detecting contamination by an amplicon from a previous amplification reaction, said method comprising the steps of:

conducting a control nucleic acid amplification reaction in a sample in a control sample comprising a nucleic acid template, using at least one primer that is capable of amplifying a detection sequence but not said template, said detection sequence having been incorporated in an amplicon of a previous amplification reaction conducted in a sample different from said control sample, using at least one chimeric primer comprising said detection sequence at a 5' end of said at least one chimeric primer; and

determining whether said sample has been contaminated by said previous amplification reaction by determining whether said control reaction produces an amplicon.

17. The method of claim 16, wherein said at least one primer in said control reaction is not complementary to any contiguous nucleic acid sequence in said template.

18. The method of claim 16, wherein said at least one primer in said control reaction is substantially complementary to said detection sequence.

19. The method of claim 16, wherein said at least one primer in said control reaction is substantially identical to said detection sequence.

20. The method of claim 16, wherein said at least one primer in said control reaction further comprises an additional sequence 3' to said detection sequence, said additional sequence being specific for a target in said previous amplification reaction.

21. The method of claim 16, wherein said detection sequence is about 20 nucleotides.

22. The method of claim 16, wherein said nucleic acid comprises DNA.

23. The method of claim 16, wherein at least one of said amplification reactions is selected from the group consisting of PCR, quantitative PCR, and reverse-transcriptase PCR.

24. The method of claim 16, wherein said determination step comprises using a sequence-specific nucleic acid probe to capture said amplicon of said control reaction.

25. The method of claim 16, wherein said sample comprises a heterogeneous population of nucleic acids.

26. The method of claim 25, wherein said sample comprises a stool sample.

27. The method of claim 25, wherein said sample comprises a blood sample.

28. (Amended) A method for detecting contamination by an amplicon from a previous sample, said method comprising the steps of:

conducting an amplification reaction in a first nucleic acid sample, using at least one chimeric primer comprising a first portion that hybridizes with at least a portion of a target nucleic acid, the amplification of which is desired, and a second, contamination detection portion that does not hybridize with said target nucleic acid;

conducting a control amplification reaction in a second nucleic acid sample different from said first nucleic acid sample, using at least one primer to amplify specifically said contamination detection portion of said chimeric primer; and

determining whether said second sample has been contaminated by an amplicon from said first sample by determining whether said control reaction produces an amplicon.

29. The method of claim 28, wherein said second portion is 5' to said first portion in each of said at least one chimeric primers.

30. The method of claim 28, wherein said at least one primer in said control reaction is not complementary to any contiguous nucleic acid sequence in any target nucleic acid in said second sample.

31. The method of claim 28, wherein said at least one primer used in said control reaction is substantially complementary to said contamination detection portion.

32. The method of claim 28, wherein said at least one primer used in said control reaction is substantially identical to said contamination detection portion.

33. The method of claim 28, wherein at least one of said amplification reactions is selected from the group consisting of PCR, quantitative PCR, and reverse-transcriptase PCR.

34. The method of claim 28, wherein said samples comprise a heterogeneous population of nucleic acids.

35. The method of claim 34, wherein said samples comprise a stool sample.

36. The method of claim 34, wherein said samples comprise a blood sample.

37. The method of claim 28, wherein said contamination detection portion is about 20 nucleotides.

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